The value of colour Doppler sonography of the knee joint: a useful tool to discriminate inflammatory from non-inflammatory disease?

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Abstract

Objective. To determine the diagnostic value of colour Doppler ultrasound (CDUS) in patients with inflammatory arthritis (IA) vs non-inflammatory disease (e.g. OA) of the knee joint.

Methods. Standardized CDUS examinations were performed in 111 knee joints of 106 patients (70 women and 36 men) presenting with severe OA (n = 72) or confirmed IA (n = 39) of one or both knee joints to determine the degree of synovial inflammation in a semiquantitative fashion. To definitely distinguish inflammatory from non-inflammatory disease, SF was obtained from every patient within 24 h after sonography and analysed SFs containing \( \leq 1000 \) white blood cells (WBC)/\( \mu l \) were considered non-inflammatory, whereas \( \geq 5000 \) WBC/\( \mu l \) were classified as inflammatory.

Results. The CDUS sum score of OA patients was determined to be 3.3 (range 0–8). In contrast, IA patients exhibited significantly elevated synovitis score of 5.3 (range 3–9) \( (P < 0.001) \). However, high synovial CDUS activity could be observed in OA patients sporadically. Therefore, there is no definitive CDUS threshold that clearly separates OA from IA patients.

Conclusion. CDUS is a valuable instrument to assist clinicians in distinguishing OA from IA of the knee joint, but nevertheless should always be interpreted within the clinical context.

Key words: power Doppler ultrasound, knee, osteoarthritis, arthritis, synovial fluid analysis.

Introduction

The knee joint is the most affected joint in OA and is frequently involved in inflammatory diseases including RA and SpA in 30–60% of patients [1, 2]. Therefore, the evaluation of knee conditions is a major task for rheumatologists and orthopaedists.

Due to its substantial potential in the evaluation of soft tissue alterations and bony changes, ultrasonography is increasingly used as a diagnostic tool. Capsule distension can be readily detected by B-mode scanning. However, capsule distension can be observed in various conditions affecting the joint and is therefore considered a non-specific feature. Colour/power Doppler ultrasound (CDUS) is able to quantify intrasynovial blood flow as a sign of inflammation of the synovial membrane and can also visualize treatment responses [3]. Therefore, CDUS appears to be superior in assessing arthritis in a quantitative fashion.

Inflammation plays a major role in arthritic disease; however, inflammatory events have also been linked to OA, and synovial hypertrophy is very common and seems to be related to pain and progression of structural damage [4–6]. Therefore, the question arises of whether there is a distinct difference between the colour/power Doppler findings in inflammatory arthritis (IA) compared with OA of the knee that allows discrimination of these conditions. Therefore, the objective of the present study was to determine the value of CDUS in the assessment of inflammatory vs non-inflammatory disease of the knee joint.
Patients and methods

Patients

A total of 111 knee joints in 106 patients (71 women and 35 men) were investigated in the study (OA: n = 72, IA: n = 39). The mean age of patients was 64 years (range 22–85): 68 years (range 47–84) in the OA group and 56 years (range 26–85) in the IA group. Patients with primary knee OA fulfilling the ACR criteria (1986) with longstanding disease without a history of inflammatory joint disease who were scheduled for knee replacement surgery were enrolled. The study was approved by the local ethics committee of the University of Regensburg.

The IA cohort consisted of patients with established inflammatory disease and clinically obvious knee effusion. In detail, 30 RA patients (according to the ACR criteria of 1987), 3 patients suffering from PsA (according to the CASPAR criteria of 2005), 2 patients with gout, 2 patients suffering from JIA and 1 patient with Lyme arthritis were enrolled in this study.

SF analysis

All patients underwent SF analysis to distinguish between inflammatory and non-inflammatory arthropathies and to identify OA patients with hidden inflammatory knee arthritis due to yet unknown microcrystal disease. As knee effusions caused by OA usually contain a low cell count of approximately 200 leucocytes/μl, WBC < 1000/μl was considered as non-inflammatory, whereas WBC ≥ 5000/μl was classified as definitely inflammatory reflecting IA as underlying condition.

Ultrasonographic assessment

US was performed by two sonographers (W.H. and N.B.) with longstanding experience in musculoskeletal US within 24 h before arthrocentesis or knee surgery. The investigators were blinded to the result of the SF analyses. Informed consent for the study was obtained before the examination. Logiq 7 equipment from GE (General Electric Healthcare, Chalfont St Giles, UK) with a linear multifrequency probe (M12L) with 5–14 MHz frequency and a field of view of 40 mm was used. The technical parameters of the examination included pulse repetition frequency of 700 Hz, colour Doppler frequency of 6.7 MHz, highest gain level without background noise and high colour persistence and a low wall filter.

The knee was examined with the patient in the supine position in four different planes: the suprapatellar longitudinal scan, the infrapatellar longitudinal scan, the medial and the lateral longitudinal scan. In each scan, colour Doppler activity was semi-quantitatively scored as follows: grade 0 = no intra-articular colour signal, grade 1 = up to three single colour signals or two single colour signals and one confluent colour signal representing only low flow, grade 2 = greater than grade 1 to <0.50% of the intra-articular area filled with colour signals representing clear flow and grade 3 = >0.50% of the intra-articular area filled with colour signal. Then a PDUS sum score (range 0–12) was calculated for each patient.

Statistical analysis

Statistical analysis was performed with SPSS statistical software, version 19 (SPSS, Chicago, IL, USA). For quantitative parameters (e.g. age of examined patients and CDUS scores), the median and range were reported. Significant differences were detected using non-parametric Mann–Whitney U test. P-values <0.05 were considered statistically significant. Receiver operating characteristic (ROC) analyses comparing the ability of the individual CDUS scores and the CDUS sum score to detect IA were additionally performed.

Results

Overall, there was a significantly lower total colour Doppler score in OA patients presenting with a non-inflammatory knee condition compared with IA patients [3.3 (range 0–8) vs 5.3 (range 0–9); P < 0.001]. The highest individual scores were observed in the lateral longitudinal scan in the cohort of OA as well as IA patients. Table 1 depicts the distribution of the colour Doppler activity, and Fig. 1 shows the distribution of the CDUS sum score. However, a relatively high CDUS score of >5 was observed in 11 OA patients, whereas 14 IA patients had a CDUS score ≤5. Therefore, a definitive CDUS threshold could not be calculated that clearly separates OA from IA patients. Detailed clinical data including the results of the SF analysis are depicted in supplementary Table S1 (available at Rheumatology Online).

A ROC analysis using the CDUS sum score to detect IA revealed an area under the curve (AUC) of 0.787 (95% CI 0.699, 0.874), which was numerically higher than the AUC of the individual CDUS scores: the suprapatellar longitudinal scan AUC 0.714 (95% CI 0.607, 0.822), the infrapatellar longitudinal scan AUC 0.602 (95% CI 0.487, 0.717), the medial scan AUC 0.735 (95% CI 0.641, 0.828) and the lateral longitudinal scan AUC 0.667 (95% CI 0.559, 0.776). Selecting a cutoff with a high sensitivity (CDUS sum score ≥3) revealed a sensitivity of 100.0% with a specificity of 68.1% for detecting IA, and selecting a cutoff with high specificity (CDUS sum score ≥6) revealed a

### Table 1 CDUS scores of the patients with OA vs arthritis of the knee

<table>
<thead>
<tr>
<th>Scan</th>
<th>OA patients (n = 73)</th>
<th>IA patients (n = 39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suprapatellar</td>
<td>0.0; 0.14 (0–2)</td>
<td>1.0; 0.64 (0–2)</td>
</tr>
<tr>
<td>Infrapatellar</td>
<td>0.0; 0.14 (0–2)</td>
<td>0.0; 0.44 (0–2)</td>
</tr>
<tr>
<td>Medial longitudinal</td>
<td>1.0; 1.2 (0–3)</td>
<td>2.0; 2.0 (1–3)</td>
</tr>
<tr>
<td>Lateral longitudinal</td>
<td>2.0; 2.0 (0–3)</td>
<td>2.0; 2.3 (1–3)</td>
</tr>
<tr>
<td>Total score</td>
<td>3.0; 3.3 (0–8)</td>
<td>5.0; 5.3 (3–9)*</td>
</tr>
</tbody>
</table>

Values are presented as median; mean (range). *Mann-Whitney U test: P value < 0.001.
specificity of 95.8% with a sensitivity of 41.0% for detecting IA. For CDUS sum scores of <3, the positive predictive value for OA was 23/23 (100.0%), while for a CDUS sum score of ≥6 the positive predictive value for IA was 16/19 (84.2%) in our cohort.

Discussion

In the past 10 years, CDUS has proved to be a suitable imaging tool by providing information about the presence and the extent of synovitis in arthritis and OA of the knee [7, 8]. PDUS findings demonstrate a strong correlation to histopathology as shown by several authors [7, 9]. Recently, published data by Takase et al. [10] revealed that PDUS visualized pathologically active synovitis even more specifically than MRI. However, to our knowledge, this is the first study that directly compares the amount of CDUS activity in OA vs IA of the knee joint.

The present study clearly demonstrates that there is a highly significant difference between the CDUS total scores of patients suffering from severe OA compared with IA of the knee joint. In line with the presented results, the subgroup with histology-proven synovial proliferation (eight in the RA group and one in the OA group) had a statistically significantly higher degree of perfusion than the histology-negative patients in a small pilot study analysing ultrasonography and histology [7]. In addition, the highest scores were determined in the lateral longitudinal scan, which is consistent with our findings. In the above-mentioned study by Takase et al. [10], the knees of 10 RA and 5 OA patients were investigated, however, without a comparison between these groups.

Although a clear difference in total CDUS scores was observed in our cohort, a distinct threshold that definitely separates inflammatory from non-inflammatory knee conditions cannot be determined. Relatively high CDUS scores of ≥5 were observed in 11 OA patients, whereas 14 IA patients had a CDUS score of <5. However, the majority of OA patients presented with a score of <3, which was not detected in a single patient of the IA subgroup. Thus, a CDUS sum score of ≥3 has a sensitivity of 100% for IA with a still acceptable specificity of nearly 70%.

Since knee replacement surgery had been performed only in OA patients the day after the sonography, histology was not available for the IA patients. Therefore, SF analysis was performed in each patient to definitely distinguish inflammatory from non-inflammatory knee pathology. According to the literature, WBC <2000/µl should be considered as non-inflammatory [11, 12]. In line with this recommendation, knee effusions caused by OA usually contain a low cell count of approximately 200 leucocytes/µl [12]. To utilize synovial analysis as a gold standard and allow for a distinct separation between the two subgroups, WBC <1000/µl was considered to be non-inflammatory, whereas WBC >5000/µl was classified as definitely inflammatory. One patient suffering from RA presenting with knee effusion had a very low WBC count with only 100 leucocytes/µl and was therefore classified as non-inflammatory despite the diagnosis of RA. However, none of the OA patients presented with WBC >1000/µl, confirming the strict differentiation of these two study groups.

One major limitation of the study relates to the clinical information available to the investigator, since sonographers were blinded only regarding the results of the SF analysis but might be aware of the clinical diagnosis. This may have caused a certain observer bias. However, patients were enrolled to one of the subgroups according the results of the synovia analysis, which were not available to the investigators at the time CDUS was performed.

In summary, CDUS seems to be a valuable tool to assist clinicians in distinguishing OA from IA of the knee joint. Lacking a clear threshold, the individual colour Doppler sonography finding alone might be misleading and has to be interpreted together with grey-scale US findings within the clinical context.

Rheumatology key messages

- PDUS is a useful tool to distinguish inflammatory from non-inflammatory knee swelling.
- There is no definitive PDUS threshold to allow for discrimination of inflammatory and non-inflammato-ry joint disease.

Disclosure statement: The authors have declared no conflicts of interest.

Supplementary data

Supplementary data are available at Rheumatology Online.
References


